(GenBank Accession No. U18799), in view of Taylor et al. (1999), Milner et al. 1997), Baracchini et al. (US Patent 5,821,154), and Hayes et al. (1998) has been maintained. Applicants believe that the Examiner has meant to maintain the rejection of all pending claims, including claim 15. Accordingly, Applicants have responded to the Office Action assuming that the rejection pertains to claims 1, 2 and 4-15.

The Examiner suggests that it would have been *prima facie* obvious to one of ordinary skill to design and use antisense for inhibition of damage-specific DNA binding protein 1, P127 expression since the sequence was taught by Dualan et al., and since Taylor et al. teaches antisense oligonucleotides can be designed to inhibit any gene of known sequence. The Examiner suggests that motivation is provided by Hayes et al. in teaching the role of this gene in repair of DNA damage, while Baracchini et al. teach the claimed modifications. Further, the Examiner suggests that Milner et al. provide a reasonable expectation of success because they teach methods for screening for antisense activity. The Examiner states that Applicants arguments set forth in the previous response are not persuasive and that the burden of proof is on the Applicants to show that the claimed compounds are not obvious. Applicants respectfully traverse the rejection.

Dualan et al. disclose the sequence of a damage-specific DNA binding protein of a sequence referred to by GenBank Accession No. as U18299. Although this sequence is the same as the damage-specific DNA binding protein 1, P127 gene cited and claimed as a target for antisense in claims 1, 2 and 4-15, this reference does not teach or suggest targeting this gene with antisense compounds as claimed. Therefore, this primary reference fails to teach the limitations of the claims as filed.

The secondary references cited, when combined with this primary reference, fail to overcome the deficiencies in teaching of this primary reference.

Taylor et al. (1999) discuss the use of antisense as a way to determine function of genes. Although this paper states that antisense can be designed to inhibit any gene whose sequence is known, this paper does NOT state that such antisense are expected to inhibit gene expression. It is only with testing of the individual antisense compound, such as are provided for in the instant specification, that one can know if antisense compounds specific to this gene target, damage-specific DNA binding protein 1, P127, are capable of inhibiting gene expression. Moreover, nowhere does this reference teach or suggest antisense compounds of any type targeted to damage-specific DNA binding protein 1, P127

nucleic acid molecules as claimed. Therefore, this reference also fails to teach the limitations of the instant claims.

Milner et al. teach a method for identifying antisense oligonucleotides using optimization techniques where the antisense oligonucleotides have 1-17 bases and target sequences of a gene. However, nowhere does this paper teach or suggest antisense oligonucleotides 8 to 50 nucleobases in length targeted to damage-specific DNA binding protein 1, P127 nucleic acid molecules as claimed.

Baracchini et al. (US Patent 5,801,154) teaches methods of modifying antisense oligonucleotides to enhance activity. However, nowhere do this patent teach or suggest antisense oligonucleotides 8 to 50 nucleobases in length targeted to damage-specific DNA binding protein 1, P127 nucleic acid molecules as claimed.

Hayes et al. (1998) disclose the role of p48 subunit binding to E2F1, making p48 a target for E2F regulation. Nowhere does this paper teach or suggest a role for the p127 subunit. Since the present invention is directed to antisense oligonucleotides 8 to 50 nucleobases in length targeted to damage-specific DNA binding protein 1, P127 nucleic acid molecules, this paper fails to provide any motivation for one of skill to combine this reference with

others in order to establish a *prima facie* case of obviousness for antisense compounds as claimed.

Therefore, contrary to the Examiner's suggestion, this combination of art, when considered together, fails to teach the limitations of the claims as filed which are limited to antisense compounds targeted to damage-specific DNA binding protein 1, P127, compounds that specifically hybridize with and inhibit the expression of damage specific DNA binding protein 1, P127.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim antisense compounds targeted to the damage-specific DNA binding protein 1, P127 of SEQ ID NO: 3. A mere teaching of antisense in general does not render obvious the development of specific antisense compounds targeted to a specific sequence. The fact that the Examiner has cited the sequence of a damage-specific DNA

protein is not appropriate for making a case for obviousness. Further, the motivation to combine references must be provided by the references themselves, not by the teaching of the instant specification (see MPEP 2143.01), and it only with the specification in hand that one of skill would be motivated and expect success in making antisense compounds as claimed and taught in the specification as filed. Thus, this combination of art cannot render the instant claimed invention obvious.

However, in an earnest effort to advance the prosecution, Applicants have canceled claim 11 and amended claim 1 to recite that the antisense compounds of the instant invention are targeted to specific regions within the sequence of damage-specific DNA binding protein 1, P127 (SEQ ID NO: 3). Support for these amendments can be found throughout the specification as filed, but in particular at pages 80-83. Nowhere in the cited references, either alone or when combined, are these regions of damage-specific DNA binding protein 1, P127 (SEQ ID NO: 3) taught or suggested as being successful targets for antisense. It is only with the specification in hand that one of skill would see that each of the claimed regions are active areas to be targeted successfully with antisense. Accordingly, withdrawal of this rejection is therefore respectfully requested based on these amendments to the claims.

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II. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

Date: March 3, 2003

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 1 has been canceled without prejudice.

Claim 1 has been amended as follows:

1. (amended) A compound 8 to 30 nucleobases in length targeted to a 5'-untranslated region, a start codon region, a coding region, a stop codon region, or a 3'-untranslated region of a nucleic acid molecule encoding Damage-specific DNA binding protein 1, p127 (SEQ ID NO: 3) wherein said compound specifically hybridizes with and inhibits the expression of Damage-specific DNA binding protein 1, p127.